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US 5976234	USP 19991102	11
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US 4976736	USP 19901211	8
US 4794171	USP 19881227	11
US 4222128	USP 19800916	5

United States Patent

Chow et al.

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[54] SELF-SETTING CALCIUM PHOSPHATE CEMENTS AND METHODS FOR PREPARING AND USING THEM

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[73] Assignee: American Dental Association Health Foundation, Gaithersburg, Md.

[*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: 08/846,145

[22] Filed: Apr. 25, 1997

Related U.S. Application Data

[60] Continuation of application No. 08/478,670, Jun. 7, 1995, abandoned, which is a division of application No. 08/126,502, Sep. 24, 1993, Pat. No. 5,525,148

[51] Int. Cl.⁵ C09K 3/00

[52] U.S. Cl. 106/35; 106/690; 106/691; 106/792; 623/16; 433/201.1

[58] Field of Search 106/35; 690, 691; 106/692; 623/16; 433/201.1

References Cited

U.S. PATENT DOCUMENTS

33,161 2/1861 Brown et al.
33,221 5/1861 Brown et al.
3,679,360 7/1972 Rubin et al.
3,787,900 1/1974 McGee
3,913,229 10/1975 Drakell et al.
3,929,971 12/1975 Roy
4,067,935 7/1978 Janko
4,467,075 2/1985 Niwa et al.
4,599,085 7/1986 Riess et al.
4,880,610 11/1989 Constantz
5,024,059 7/1991 Constantz
5,047,031 9/1991 Constantz
5,053,212 10/1991 Constantz et al.
5,129,905 7/1992 Constantz
5,336,264 8/1994 Constantz et al.
5,453,231 10/1995 Constantz et al.

5,456,359 3/1996 Ison et al.
5,525,148 6/1996 Chow et al. 106/35

FOREIGN PATENT DOCUMENTS

4-16761A1 3/1991 European Pat. Off.
9503369 2/1995 European Pat. Off.

OTHER PUBLICATIONS

Kenney, et al., (1988): The Use of a Porous Hydroxyapatite Implant in Periodontal Defects, *J. Periodontol.*, pp. 67-72, Feb. 1988.
Zide, et al., (1987): Hydroxyapatite Cranioplasty Directly Over Dura, *J. Oral Maxillofac. Surg.* 45:481-486, 1987.
Waite, et al., (1986): Zygomatic Augmentation with Hydroxyapatite, *J. Oral Maxillofac. Surg.* 44:343-352, 1986.
Verwoerd, et al., (1987): Porous Hydroxyapatite-perichondrium Graft in Cricoid Reconstruction, *Acta Otolaryngol (Stockh)* 103:496-502.
Grote, (1984): Tympanoplasty with Calcium Phosphate, *Arch Otolaryngology* 110:197-199, 1984.
Kent, et al., (1983): Alveolar Ridge Augmentation Using Nonresorbable Hydroxyapatite with or without Autogenous Cancellous bone, *J. Oral Maxillofac. Surg.* 41:629-642, 1983.

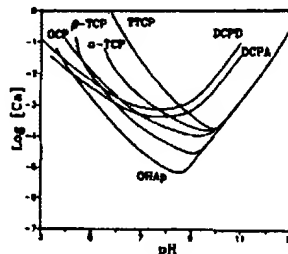
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ABSTRACT

The invention includes methods and compositions relating to calcium phosphate cements, which self-harden substantially to hydroxyapatite at ambient temperature when in contact with an aqueous medium. More specifically the cements comprise a combination of one or more sparingly soluble calcium phosphates other than tetracalcium phosphate with an aqueous solution adjusted with a base to maintain a pH of about 12.5 or above and having sufficient dissolved phosphate salt to yield a solution mixture with phosphate concentration equal to or greater than about 0.2 mol/L.

22 Claims, 1 Drawing Sheet



EAST search

3/29/01

best art

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4	US	5397362	USP:19950314	5	Imp
5	US	4976736	USP:19901211	8	Coa
6	US	4794171	USP:19881227	11	Cal
7	US	4222128	USP:19800916	5	Com

(12) **United States Patent**
Brown et al.

(10) Patent No.: **US 6,201,039 B1**
(45) Date of Patent: ***Mar. 13, 2001**

(54) **BONE SUBSTITUTE COMPOSITION
COMPRISING HYDROXYAPATITE AND A
METHOD OF PRODUCTION THEREFOR**

(75) Inventors: Paul W. Brown, State College, PA (US); Kevor S. Ten Huisen, Nesbanic Station, NJ (US); Roger I. Martin, Denver, PA (US)

(73) Assignee: The Penn State Research Foundation, University Park, PA (US)

(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 00 days.

(21) Appl. No.: 08/617,809

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Related U.S. Application Data

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(51) Int. Cl. ⁷ A61F 2/28

(52) U.S. Cl. 523/115; 424/423

(58) Field of Search 424/423; 523/115, 523/116

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,767,437 • 10/1973 Cruz, Jr.
3,928,971 • 12/1975 Roy
4,548,959 • 10/1985 Nagai et al.
4,793,467 • 1/1989 Piaz et al.
5,496,399 3/1996 Ison et al.

FOREIGN PATENT DOCUMENTS

1-111762 4/1989 (JP).

OTHER PUBLICATIONS

Thesis, The Formation of Biocomposites at Physiological Temperatures, Kevor S. Ten Huisen, The Pennsylvania State University, Shelved Nov. 18, 1992.

TenHuisen et al., Journal of Biomedical Materials Research, vol. 28, 27-33 (1994).

* cited by examiner

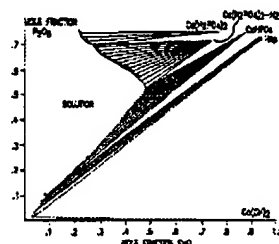
Primary Examiner—Carlos Azpuru

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(57) **ABSTRACT**

The present invention is directed to polymineralic particles which are precursors of hydroxyapatite and a method for their production. The present invention is also directed to a synthetic bone-like composition comprising said hydroxyapatite polymineralic precursor particles of hydroxyapatite and optionally, a polymeric material capable of promoting mineralization of hydroxyapatite, which are useful for fixing prosthetic devices, useful as bone substitutes to directly fill bone defects, to provide substrates for cartilage, and to repair teeth, and methods of making such preparations. The present invention is also directed to a method of treating collagen to provide a micro-structure close to that of native bone.

22 Claims, 5 Drawing Sheets



THE FIGURE IS A GRAPH OF Wt. Fraction P2O5 vs. Wt. Fraction CaO. The Y-axis is labeled 'Wt. Fraction P2O5' and ranges from 0 to 1.0. The X-axis is labeled 'Wt. Fraction CaO' and ranges from 0 to 1.0. A diagonal line from (0,0) to (1,1) is labeled 'SOLUBLE'. A shaded region above this line is labeled 'SOLUBLE'. A point on the diagonal is labeled 'CaO/P2O5 = 1.0'. A point above the diagonal is labeled 'CaO/P2O5 = 1.667'. A point below the diagonal is labeled 'CaO/P2O5 = 0.5'. A point on the diagonal is labeled 'CaO/P2O5 = 1.0'.